UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,115	11/25/2003	Steven D. Girouard	279.597US1	4851

21186 7590 04/01/2009
SCHWEGMAN, LUNDBERG & WOESSNER, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

EXAMINER	
BEISNER, WILLIAM H	

ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
04/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/722,115	GIROUARD ET AL.	
	Examiner	Art Unit	
	WILLIAM H. BEISNER	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-14,73-79 and 81-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-14,73-79 and 81-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/17/2009 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-10, 12-14, 73-79 and 81-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dennis et al.(US 6,114,164) in view of Kofidis et al.(Journal of Thoracic and Cardio. Surg.), Farb et al.(US 6,048,722), Bursac et al.(Am. J. Physiol. 277) and Terracio et al.(In Vitro Cell. and Develop. Bio.).

The reference of Dennis et al. discloses an apparatus for emulating an in vivo environment that includes a culture module (38) to host cells and culturing medium, an electrical stimulator (14) coupled to the culturing module (38), a stress simulator (16, 18, 26, 30, 40) coupled to the culturing module and a controller (20) coupled to the electrical stimulator (14) and stress simulator (16, 18, 26, 30, 40) (See Figure 1).

Claim 1 differs by reciting that the device includes a biological treatment administration module coupled to the culture module and controller.

The reference of Kofidis et al. discloses that it is known in the art to not only mechanically stimulate cardiac cells in vitro but to also chemically stimulate the cells in vitro (See page 65, column 1, first paragraph).

The reference of Farb et al. discloses that biological treatment administration modules (14) are known in the art for automating the introduction of various chemical stimuli with respect

to a biological material (32). The module (14) is coupled to a cell holding chamber (12) and controller (10).

In view of these teachings, it would of have been obvious to one of ordinary skill in the art to modify the device of the primary reference to include a biological treatment administration module for the known and expected result of allowing any cells cultured in the device of the primary reference to be additionally chemically stimulated as suggested by the reference of Kofidis et al. while allowing the automation of all the stimulation structures and detection devices.

While the reference of Dennis et al. states that the system is "for adaptively controlling a muscle tissue specimen in order to emulate its in vivo environment", Claim 1 further differs by requiring that the claimed electrical stimulator is "adapted to create cardiac electrical conditions in the culturing medium, the cardiac electrical conditions simulating electrical conditions in the myocardium that result in cardiac contraction".

The reference of Bursac et al. discloses that when culturing cardiac cells *in vitro* it is known in the art to electrically stimulate the cells using electrodes wherein the electrodes provide pacing impulses at a rate of 60 beats/min (See page H436 "Electrophysiological Assessment" and Figure 1B).

In view of this teaching, when culturing cardiac cells in the device of the primary reference of Dennis et al., it would have been obvious to one of ordinary skill in the art to "adapt" the electrical stimulator to provide the pacing disclosed by the reference of Bursac et al. as is conventional in the art for electrically stimulating cardiac cells *in vitro* and emulating an in vivo environment as is required of the reference of Dennis et al.

While the reference of Dennis et al. states that the system is "for adaptively controlling a muscle tissue specimen in order to emulate its in vivo environment", Claim 1 further differs by requiring that the claimed stress stimulator is "adapted to create a mechanical stress upon the cells, the mechanical stress simulating a tension applied upon cardiac muscle cells in the myocardium".

The reference of Terracio et al. discloses that it is conventional in the art to mechanically stimulate cardiac cells while cultured in vitro to expose the cells to tension found in vivo (See the abstract).

In view of this teaching, when culturing cardiac cells in the device of the primary reference of Dennis et al., it would have been obvious to one of ordinary skill in the art at the time the invention was made to "adapt" the mechanical stimulator to provide the mechanical tension disclosed by the reference of Terracio et al. as is conventional in the art for mechanically stimulating cardiac cells in vitro and emulating an in vivo environment as is required of the reference of Dennis et al.

With respect to the claim limitation that the biological treatment administration module "including one or more biological agents selected from protein and nucleic acid", the modules resulting from the combination of the reference of Farb et al. with Dennis et al. would result in a structure that is capable of holding a protein or nucleic acid agent that can be communicated with the culturing module. Note positive recitation in the claims that the apparatus includes a protein or nucleic acid agent does not further patentably distinguish the structure of the claim because "Expressions relating the apparatus to contents thereof during an intended operation are of no significance in determining patentability of the apparatus claim." Ex parte Thibault,

164 USPQ 666, 667 (Bd. App. 1969). See MPEP 2115.

With respect to the claimed "memory circuit" and "controller", the reference of Dennis et al. discloses a controller and user interface (52) that includes input devices, memory and display which allow manipulation of the conditions within the system. The additional references as discussed in the rejection of record provide the motivation for controlling the different stimulation devices for emulating the conditions found in vivo. As a result, an apparatus programmed as suggested in the rejection of record would meet the memory circuit limitations of amended claims 1

With respect to claim 2, the reference of Dennis et al. discloses electrodes (22) in the culture chamber. The reference of Bursac et al. also discloses the use of electrodes in the culture medium (See Figure 1b).

With respect to claims 3 and 4, the reference of Bursac et al. discloses that the electrodes function as a pacemaker to pace the tissue as found in vivo. The electrodes also generate an electric field.

With respect to claims 5, 6 and 74, the reference of Terracio et al. discloses culturing cardiac cells on a deformable silicone substrate when exposing the cells to mechanical stimulation (See page 53, second column) using the mechanical linkage disclosed in Figure 1.

With respect to claim 7, the device of Dennis et al. includes a variable speed motor (16) and mechanical linkage (40, 30). The reference of Terracio et al. also discloses the use of a variable speed motor and mechanical linkage (See Figure 1).

With respect to claims 8 and 75, the reference of Farb et al. discloses one or more chemical dispensers (18).

With respect to claim 9, the reference of Dennis et al. discloses a fluid perfusion system that would function as a mixer (See column 5, lines 35-38).

With respect to claims 10, 12 and 73, the reference of Dennis et al. discloses a user interface (52) that includes input device, memory and a display which allow manipulation of the conditions within the system.

With respect to claims 13 and 14, the reference of Terracio et al. also discloses that microscopic observation of the cells is conventional in the art (See page 53, second column) and would have been within the purview of one having ordinary skill so as to observe the cultured cells.

With respect to claims 76-78, the controller resulting from the combination of the references discussed in the rejection are structurally capable of providing the control and/or processing required of claims 76-78.

With respect to claim 79, the reference of Farb et al. discloses the use of imaging devices for monitoring the medium application zone (See column 9, lines 1-15) is conventional in the art and would have been obvious for the known and expected result of visually monitoring the tissue during the processing steps.

With respect to claims 81-84, positive recitation in the claims that the apparatus includes a protein or nucleic acid agents does not further patentably distinguish the structure of the claim because "Expressions relating the apparatus to contents thereof during an intended operation are of no significance in determining patentability of the apparatus claim." Ex parte Thibault, 164 USPQ 666, 667 (Bd. App. 1969). See MPEP 2115.

Response to Arguments

6. With respect to the rejection of claim 1 over the combination of the references of Dennis et al.(US 6,114,164) in view of Kofidis et al.(Journal of Thoracic and Cardio. Surg.), Farb et al.(US 6,048,722), Bursac et al.(Am. J. Physiol. 277) and Terracio et al.(In Vitro Cell. and Develop. Bio.), Applicants argue (See pages 6-8 of Applicants' response filed 2/17/2009) that the rejection is improper for the following reasons:

> i) *Applicant respectfully traverses the rejection and submits that the Office Action does not set forth a proper prima facie case of obviousness because the cited portions of Dennis, Kofidis, Farb, Bursac, and Terracio, individually or in combination with each other and reasoning given in the Office Action, do not provide the claimed subject matter. For example, Applicant is unable to find in the cited portions of Dennis, Kofidis, Farb, Bursae, and Terracio, individually or in combination, among other things, one or more biological stimulus agents selected from protein and nucleic acid, and a biological treatment administration module including the one or more biological stimulus agents, as recited in claim 1. Applicant is unable to find in the Office Action a proper reason that remedies this deficiency of the cited references.*
>
> *The Office Action cites Exparte Thibault, 164 USPQ 666, 667 (Bd. App. 1969), as cited in MPEP 2115, to support an assertion that "positive recitation in the claims that the apparatus includes a protein or nucleic acid agent does not further patentably distinguish the structure of the claim". However, MPEP 2115 states "that this line of cases is limited to claims directed to machinery which works upon an article or material in its intended use." The biological treatment administration module does not work upon the one or more biological stimulus agents selected from protein and nucleic acid as recited in claim 1. Therefore, it is believed that Exparte Thibault and MPEP 2115 do not apply.*
>
> *The Advisory Action asserts:*
>
> *It is fundamental that an apparatus claim defines the structure of the invention and not how the structure is used in a process, or what materials the structure houses in carrying out the process. (Citations omitted.) As long as the apparatus of combination of the references recited in the rejection is capable of administering a biological stimulus agent, the prior art device meets the requirements of the claimed feature. Applicant has*

> *not established on this record any structural distinction between apparatus within the scope of the instant claim and the device encompassed by the combination of the references set forth in the prior art rejection of record.*
>
> *Claim 1 has been amended to further clarify that the one or more biological stimulus agents are recited as a structural limitation, rather than what the recited biological treatment administration module is "adapted to include" or "capable of holding". Claim 1 differs from the combination of the cited references in that the claimed biological treatment administration module includes, as part of the structure, the one or more biological stimulus agents selected from protein and nucleic acid.*

In response to comment i) above and as previously noted in the final office action, it is fundamental that an apparatus claim defines the structure of the invention and not how the structure is used in a process, or what materials the structure houses in carrying out the process. Exparte Masham, 2 USPQ2d 1647, 1648 (BPAI 1987). See also In re Yanush, 477 F.2d 958, 959, 177 USPQ 705,706 (CCPA 1973); In re Finsterwalder, 436 F.2d 1028, 1032, 168 USPQ 530, 534 (CCPA 1971); In re Casey, 370 F.2d 576, 580, 152 USPQ 235,238 (CCPA 1967). As long as the apparatus of combination of the references recited in the rejection is capable of administering a biological stimulus agent, the prior art device meets the requirements of the claimed feature. Applicants have not established on this record any structural distinction between apparatus within the scope of the instant claims and the device encompassed by the combination of the references set forth in the prior art rejection of record. The Examiner recognizes that the biological stimulus agents have been positively recited as part of the claimed device but, as stated previously, the positive recitation of the agents fails to patentably distinguish the claimed apparatus over that of encompassed by the combination of the references discussed previously for the same reasons set forth in *Exparte Thibault; Exparte Masham; In re Yanush; In re Finsterwalder; and In re Casey.*

ii) *Applicant also respectfully submits that the Office Action has not provided a properly articulated reason for combining Dennis, Kofidis, Farb, Bursac, and Terracio. The devices in Dennis and Terracio are to mimic in vivo mechanical and electrical, or mechanical, respectively, stimuli for in vitro analyses of certain cell types. The devices in Farb and Bursac are to measure in vitro electrophysiological responses of cells such as microeletrode impaled or cannula ruptured oocytes or rat ventricular cells and cardiac myocytes after perfusion of agents to study membrane physiology or after electrical stimulation for in vitro impulse propagation studies, respectively. In Kofidis, calcium and epinephrine, as well as electrical stimulation or stretching, are applied to collagen matrices with spontaneously beating cardiomyocytes, to enhance force development. As each device in Dennis, Kofidis, Farb, Bursac, and Terracio is designed for a particular purpose, there is no proper reason for combining Dennis, Kofidis, Farb, Bursac, and Terracio to arrive at a device to prepare cells for in vivo administration and long term maintenance by stimulating cells ex vivo prior to cell therapy with a cardiac electrical stimulator, a myocardial stress simulator, and a biological stimulus that enhances one or more of engraftment, survival, and differentiation of the cells, wherein the biological stimulus agent is a protein or nucleic acid.*

In the Advisory Action, it is stated that:

As long as the apparatus of combination of the references recited in the rejection is capable of administering a biological stimulus agent, the prior art device meets the requirements of the claims feature.

Only Kofidis and Farb disclose adding a chemical agent to cells. Kofidis mounted strips of collagen cultured with cardiomyocytes to the side of a chamber that was filled with culture medium, and calcium and epinephrine were added to the culture medium. Thus, the device of Kofidis apparently does not include a biological treatment administration module coupled to a culturing module. Farb disclose a series of receptacles for chemical agents for delivery to a cell linked to impaling electrodes or delivery via a membrane piercing cannula. Therefore, the device of Farb, while capable of delivering a biological stimulus agent, does not provide an environment that produces cells with long term viability, e.g., those for cell therapy, as the cells are either impaled with microelectrodes or with a cannula that introduces agents into the cytoplasm.

Additionally, Applicant respectfully submits that the Office Action has not provided a rationale for which one of ordinary skill in the art would have had reasonable expectation of success in the combination of the cited references. For example, Applicant is unable to find in the cited references and the Office Action a reason for expecting the delivery of the electrical stimuli, the mechanical

stimuli, and the biological stimuli to produce an additional benefit relative to the delivery of a subset thereof. Applicant respectfully requests such a rationale, or withdrawal of the rejection.

In response to comment ii) above, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the reference of Kofidis et al. discloses that it is known in the art to not only mechanically stimulate cardiac cells in vitro but to also chemically stimulate the cells in vitro (See page 65, column 1, first paragraph) and the reference of Farb et al. discloses that biological treatment administration modules (14) are known in the art for automating the introduction of various chemical stimuli with respect to a biological material (32). The module (14) is coupled to a cell holding chamber (12) and controller (10). The examiner is of the position that in view of these teachings, it would of have been obvious to one of ordinary skill in the art to modify the device of the primary reference to include a biological treatment administration module for the known and expected result of allowing any cells cultured in the device of the primary reference to be additionally chemically stimulated as suggested by the reference of Kofidis et al. while allowing the automation of all the stimulation structures and detection devices.

Additionally, the Examiner is of the position that the rational provided in the rejection of the claims meets the requirements set forth in rational A) for establishing a prima facie case of obviousness (See MPEP 2143). It is noted the rationale to support a conclusion that the claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no

change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art. KSR, 550 U.S. at ___, 82 USPQ2d at 1395; Sakraida v. AG Pro, Inc., 425 U.S. 273, 282, 189 USPQ 449, 453 (1976); Anderson 's-Black Rock, Inc. v. Pavement Salvage Co., 396 U.S. 57, 62-63, 163 USPQ 673, 675 (1969); Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp., 340 U.S. 147, 152, 87 USPQ 303, 306 (1950). "[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." KSR, 550 U.S. at ___, 82 USPQ2d at 1396. If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art.

iii) *Claims 2-10, 12-14, 73-79, and 81*

> *Applicant respectfully traverses the rejection. Claims 2-10, 12-14, 73-79, and 81 are dependent on claim 1, which is believed to be patentable for at least the reasons set forth above. Therefore, the discussion above for claim 1 is incorporated herein to support the patentability of claims 2-10, 12-14, 73-79, and 81.*

In response to comments iii) above, the Examiner maintains that the combination of the references previously discussed above meets the instant claims, including independent claim 1.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to WILLIAM H. BEISNER whose telephone number is (571)272-

1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/William H. Beisner/
Primary Examiner
Art Unit 1797

WHB